What Determines Mortality Risk in Male Former Cigarette Smokers?

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ABSTRACT

Objectives. The purpose of this study was to examine what factors determine the mortality experience of male ex–cigarette smokers, those who no longer smoke at all and those who changed to pipe or cigar smoking.

Methods. A cohort study was undertaken with 18-year mortality data on 19 018 men.

Results. Ex–cigarette smokers had an intermediate mortality risk compared with never and current smokers. Ex–cigarette smokers who switched to pipe smoking had higher mortality than those who no longer smoked at all. The mortality rates for pipe and cigar smokers who were former cigarette smokers were higher than those for pipe or cigar smokers who had never smoked cigarettes. Ex–cigarette smokers who consumed more than 20 cigarettes per day for more than 20 years experienced increased mortality for both coronary heart disease and neoplasms, even after 30 years of cessation.

Conclusions. These results support the notion that an elevated mortality risk may be seen for ex–cigarette smokers, even after they have given up smoking for many years. Ex–cigarette smokers who change to a pipe have a greater mortality risk than those who no longer smoke at all. (*Am J Public Health.* 1994;84:1235–1242)

Introduction

The prevalence of smoking in many populations has been falling, in particular for men.[1] An ever-increasing proportion of the general population are former cigarette smokers who have either given up smoking or changed to a pipe or cigars. Many studies have reported reduced mortality for former smokers compared with smokers.[2–9] Whether former smokers ever reach the same levels of mortality risk as never smokers remains controversial.[10–12] The mortality risk of pipe or cigar smokers may also differ depending on a past history of cigarette smoking. These issues are of importance because they may provide some insight as to etiological mechanisms, enable better predictions of future trends in mortality, and provide the public with realistic expectations of the potential benefit, in terms of the reduced risk of mortality, that has been observed from stopping smoking.

The Whitehall Study previously reported no difference in risk of death from coronary heart disease between never smokers and ex-smokers after 5 years of follow-up.[13] We re-examined data from the Whitehall study after 18 years of follow-up. Our aims were to examine the mortality risk of former cigarette smokers compared with never smokers with particular reference to duration of smoking habit, number of cigarettes consumed, change in smoking habit, and time since giving up cigarettes. We also looked at the effect of changing from cigarettes to pipe or cigar smoking.

Subjects and Methods

In the Whitehall Study, 19 018 men aged 40–69 years from the British Civil Service were examined between 1967 and 1969. The main aim of the study was to examine what risk factors may be important in the etiology of coronary heart disease, as well as other chronic diseases.[14–16] In this cohort study, all exposure data were collected only at baseline with no subsequent reassessments.

If the subjects stated at baseline that they had never smoked any form of tobacco they were classified as never smokers. If they currently smoked cigarettes they were categorized as current cigarette smokers, irrespective of whether they also smoked a pipe or cigars. If subjects did not smoke cigarettes or any other form of tobacco at baseline but had ever smoked cigarettes, they were categorized as ex–cigarette smokers. Subjects who were ex–cigarette smokers but current pipe or cigar smokers were referred to as secondary pipe or cigar smokers. Subjects who had never smoked cigarettes but were current pipe or cigar smokers were referred to as primary pipe or cigar smokers. Current smokers of both pipe and cigars were excluded so that the effects of either pipe or cigar smoking individually could be examined. Three hundred ninety-five men who were former pipe or cigar smokers and no longer smoked at all were omitted from further analysis. For both current and ex-smokers, the age when they started to

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TABLE 1—Distribution of Subjects, by Smoking Status

Smoking Status	No. (%) of Subjects
Total sample size	19 018
No data on smoking status	14
Both pipe and cigar smokers (excluded from analysis)	239
Ex–pipe or ex–cigar smokers (excluded from analysis)	395
Remaining sample size	18 370 (100)
Never smokers	3 105 (16.9)
Ex–cigarette smokers	4 833 (26.3)
Current cigarette smokers	7 921 (43.1)
Pipe smokers	1 748 (9.5)
Primary	492 (28.1)
Secondary	1 256 (71.9)
Cigar smokers	763 (4.2)
Primary	105 (13.8)
Secondary	658 (86.2)

smoke and the most they ever smoked regularly for as long as a year were ascertained. A small subsample of current cigarette smokers were later recruited into an intervention trial of smoking advice.[17]

Additional questions were asked about chest pain, respiratory symptoms, and civil service employment grade. Civil service employment grade is in four levels: administrators, professionals and executives, clerical, and "other" (mainly unskilled manual) grades. Administrators are the top grades, with the highest status and income in the civil service; the "other" grades are the lowest. For 873 subjects employed by the diplomatic service and the British Council, grades were not comparable to those for the rest of the sample. For analyses that involved grade, these subjects were kept as a separate group.

Clinical measurements included height, weight, blood pressure, forced expiratory volume in 1 second ($FEV_{1.0}$), forced vital capacity, and a limb lead electrocardiogram. An oral glucose tolerance test was administered (50 g) after an overnight fast, and a 2-hour capillary blood sample was drawn for the measurement of glucose and cholesterol concentrations.

Disease at entry was defined by any of the following: relative shortness of breath on level ground, probable or possible intermittent claudication,[18] past history of diabetes, heart or blood pressure trouble, unexplained weight loss over the preceding year, grade 1 or 2 angina according to the Rose angina questionnaire,[14] severe chest pain for over half an hour, and an abnormal resting electrocardiogram according to the following Minnesota code items: Q/QS waves (1.1–1.3); ST depressions (4.1–4.4); T-wave inversion or flattening (5.1–5.3); or left-bundle branch block (7.1). Full details of the procedures used were previously reported.[19]

Records from over 99% of subjects were flagged at the National Health Service Central Registry. Death certificates were coded according to the eighth revision of the *International Classification of Diseases* (ICD), and this almost-complete mortality follow-up to January 31, 1987, provides the basis for these analyses. Death was classified as being due to coronary heart disease (ICD codes 410–414); cardiovascular disease (ICD codes 390–458); neoplasm of trachea, bronchus, and lung (ICD code 162)—henceforth referred to as lung cancer—or any neoplasm (ICD codes 140–239); and respiratory disease (ICD codes 460–519). Neoplasms were also classified according to whether smoking is considered to play a role in their etiology.[2,5,20] The causes deemed to be smoking related are malignant neoplasms of the lip (ICD code 140), tongue (ICD code 141), mouth and pharynx (ICD codes 143–149), esophagus (ICD code 150), and pancreas (ICD code 157); respiratory system neoplasms (ICD codes 160–163) and urinary system neoplasms (ICD codes 188–189); and malignant neoplasms of unspecified site or secondary neoplasms (ICD codes 195–199). All other cancers were classified as not related to smoking.

The number of years since stopping smoking is often taken from the date of quitting up to the start of the study. That is reasonable when the period of follow-up is relatively short. With 18 years of follow-up, however, it will result in misclassification, as the number of years since stopping smoking for an ex-smoker actually increases over the follow-up period. To allow for this time dependence, the time data were analyzed by using the standard person-years approach.[21] For example, a subject aged 48 years at the start of the study who died after 13.5 years of follow-up would contribute 2 person-years to the age category 45–49 years, 5 person-years to the age categories of 50–54 and 55–59 years, and 1.5 person-years to the age category of 60–64 years. His death would be allocated to the 60–64-year category. If in fact this subject was an ex–cigarette smoker who had given up 3 years before the start of the study, then he would contribute 7 person-years to the 1–9 years since quitting cigarettes category and 6.5 person-years to the 10–19 years since quitting category, with his death being allocated to this latter category. Because of the size of the data set, person-years of observation during the 18-year follow-up were allocated on a year-by-year basis. For each year of follow-up, a new record was created consisting of each subject's current age together with baseline characteristics and length of follow-up during that year. For ex-smokers, the time since stopping smoking up to that year of follow-up was calculated as in the example above. This expanded data set was then used as the basis for all analyses of mortality.

Mortality rates were calculated by using the person-years at risk as outlined above. These rates and also all means and proportions were standardized for age by the direct method, with the total population as the standard. Differences in proportions and means in relation to smoking status were tested with the Cochran-Mantel-Haenszel statistic in SAS[22] and by analysis of covariance, respectively. Adjustment for risk factors and calculation of confidence intervals (CIs) for rate ratios were done by using Cox's proportional hazards regression model.[23] These methods are very similar to those that use Poisson regression, but they do not require the assumption of a constant hazard within the individual person-years of follow-up. Dummy variables were used in the models to assess the effects of various risk factor categories (e.g., duration of smoking, maximum amount smoked, and time since quitting) in ex–cigarette smokers compared with never smokers. Tests for linear trend in these three risk factors among ex–cigarette smokers were computed by including a dummy variable for ex–cigarette smoker and a continuous variable for the relevant risk factor. The coefficient for the continuous variable therefore represents the change in mortality per unit change in the risk factor among ex-smokers and was used as a test for trend in the risk factor. Significant departures from linearity were examined by calculating the difference for the chi-square value for heterogeneity and the chi-square value for linear trend.

TABLE 2—Age-Adjusted Mortality Rates per 1000 Person-Years, by Smoking Status

Smoking Status	Mortality Rate per 1000 Person-Years (No. of Deaths)							
	All Causes	CHD	CVD	Neoplasms				Respiratory Disease
				Total	SRN[a]	NSRN[b]	Lung Cancer	
Never smoker (n = 3105)	10.50 (421)	4.34 (175)	6.06 (240)	2.71 (111)	0.96 (49)	1.75 (72)	0.25 (24)	0.68 (24)
Ex-cigarette smoker (n = 4833)	12.10 (969)	4.72 (379)	6.48 (519)	3.74 (300)	1.51 (121)	2.23 (179)	0.73 (58)	0.95 (75)
Primary pipe (n = 492)	13.94 (113)	5.64 (46)	7.85 (64)	3.37 (27)	1.64 (13)	1.73 (14)	1.00 (8)	1.37 (11)
Secondary pipe (n = 1256)	14.12 (282)	5.92 (120)	8.13 (161)	4.20 (85)	2.43 (49)	1.77 (36)	1.18 (24)	1.00 (20)
Primary cigar (n = 105)	5.04 (9)	1.96 (4)	2.56 (5)	2.48 (4)	0.85 (2)	1.63 (2)	0.45 (1)	0.00 (0)
Secondary cigar (n = 658)	12.64 (132)	3.95 (42)	6.06 (64)	4.15 (43)	2.38 (25)	1.77 (18)	1.91 (20)	0.97 (10)
Current cigarette (n = 7921)	20.95 (2570)	7.56 (929)	10.52 (1292)	6.64 (816)	4.28 (524)	2.37 (292)	2.98 (365)	2.20 (266)

Note. CHD = coronary heart disease; CVD = cardiovascular disease; SRN = smoking-related neoplasm; NSRN = non-smoking-related neoplasm.
[a]Smoking-related neoplasms are malignant neoplasms of the lip (ICD code 140), tongue (ICD code 141), mouth and pharynx (ICD codes 143–149), oesophagus (ICD code 150), and pancreas (ICD code 157); respiratory system neoplasms (ICD codes 160–163) and urinary system neoplasms (ICD codes 188–189); and malignant neoplasms of unspecified site or secondary neoplasms (ICD codes 195–199).
[b]Non-smoking-related neoplasms were all other cancers not classified as smoking related.

For tabulations of smoking status with other baseline characteristics, the number of years since quitting at entry to the study was used instead.

Results

The different smoking categories are shown in Table 1. Of the 7921 (43.1%) men classified as cigarette smokers, 1363 (17.2%) also smoked a pipe and/or cigars. A total of 714 (9.0%) men were recruited into an intervention study and given antismoking advice. The age-adjusted mortality rates for these smoking-status groups are shown in Table 2 by cause or category of death. Current smokers had the highest mortality rates for each group of conditions. Mortality rates for ex–cigarette smokers were between those of never smokers and current smokers, although they usually were closer to the rates for never smokers. Both primary and secondary pipe smokers had significantly elevated mortality rate ratios, around 40% above those of never smokers, for all causes and coronary heart disease. Secondary pipe or cigar smokers had higher mortality compared with primary pipe or cigar smokers, but only all-cause mortality for secondary compared with primary cigar smokers was statistically significant (rate ratio = 2.30; 95% CI = 1.17, 4.52). Secondary pipe smokers did have higher

TABLE 3—Association between Smoking Habit, Years since Giving Up at Baseline, and Prevalence (%) of Preexisting Disease at the Initial Survey, Adjusted for Age

Smoking Status	Percentage of Subjects with Preexisting Disease (SE)			
	Doctor Diagnosis of High Blood Pressure or Heart Disease	Electrocardiogram Ischemia[a]	Dyspnea	Disease at Entry[a]
Never smoker	4.08 (0.40)	14.5* (0.7)	3.98** (0.39)	21.0* (0.8)
Ex–cigarette smoker	4.69 (0.30)	16.2 (0.5)	5.48 (0.32)	23.5 (0.6)
>20 y[b]	4.67 (0.61)	16.5 (1.1)	4.93 (0.69)	23.9 (1.3)
16–20 y	5.10 (0.86)	16.1 (1.4)	4.52 (0.82)	24.1 (1.7)
11–15 y	3.66 (0.68)	13.6 (1.2)	4.58 (0.76)	19.8 (1.4)
6–10 y	4.75 (0.70)	16.3 (1.2)	4.89 (0.72)	22.5 (1.4)
0–5 y	4.93 (0.58)	17.1 (1.0)	7.50 (0.70)	25.2 (1.2)
P for trend test among ex-smokers	.62	.79	<.001	.86
P for departures from trend test among ex-smokers	.50	.17	.09	.03
Current smoker	3.73** (0.21)	16.6 (0.4)	7.00*** (0.28)	25.2* (0.5)

[a]See the text for a detailed definition of this condition.
[b]Years since quitting reported at baseline, not including any follow-up period.
*P < .05; **P < .01; ***P < .001 for tests of differences in prevalence for never or current smokers compared with all ex-smokers.

mortality than ex–cigarette smokers for all-cause mortality (rate ratio = 1.17; 95% CI = 1.03, 1.34), coronary heart disease (rate ratio = 1.27; 95% CI = 1.03, 1.56), cardiovascular disease (rate ratio = 1.25; 95% CI = 1.05, 1.49), and smoking-

TABLE 4—Number of Deaths and Rate Ratio^a (95% CI) for Ex–Cigarette Smokers Compared with Never Smokers, by Amount Smoked, Duration of Smoking in Years, and Period since Quitting Cigarettes

Cause of Death	Never Smoker	Duration of Smoking, y				Rate Ratio^b per 10 y	Maximum No. of Cigarettes/d Consumed				Rate Ratio^b per 10 cigarettes/d	Years since Quitting				Rate Ratio^b per 10 y
		0–9	10–19	20–29	≥30		1–9	10–19	20–29	≥30		1–9	10–19	20–29	≥30	
All causes	421 1.00	114 1.02 (0.83, 1.25)	158 0.94 (0.78, 1.13)	307 1.29 (1.11, 1.49)	382 1.44 (1.25, 1.65)	1.15*** (1.09, 1.21)	165 1.00 (0.84, 1.20)	309 1.14 (0.98, 1.32)	313 1.32 (1.14, 1.53)	172 1.48 (1.24, 1.76)	1.11*** (1.06, 1.16)	103 1.59 (1.28, 1.98)	299 1.33 (1.15, 1.54)	274 1.13 (0.97, 1.32)	278 1.11 (0.95, 2.34)	0.91** (0.86, 0.96)
CHD	175 1.00	50 1.07 (0.78, 1.46)	63 0.90 (0.67, 1.19)	119 1.41 (1.13, 1.76)	145 1.90 (1.62, 2.24)	1.14** (1.05, 1.25)	70 1.05 (0.79, 1.38)	114 1.03 (0.82, 1.31)	127 1.32 (1.05, 1.66)	64 1.37 (1.03, 1.83)	1.12** (1.03, 1.21)	41 1.44 (1.03, 2.03)	113 1.19 (0.94, 1.50)	111 1.13 (0.89, 1.43)	113 1.15 (0.91, 1.46)	0.97 (0.89, 1.06)
Neoplasms Total	111 1.00	29 0.98 (0.65, 1.47)	52 1.17 (0.84, 1.63)	106 1.70 (1.30, 2.21)	112 1.66 (1.28, 2.17)	1.17** (1.06, 1.29)	37 0.87 (0.60, 1.26)	98 1.39 (1.06, 1.83)	105 1.71 (1.31, 2.23)	58 1.93 (1.40, 2.66)	1.16*** (1.06, 1.26)	42 2.39 (1.67, 3.42)	92 1.51 (1.15, 2.00)	86 1.37 (1.03, 1.81)	79 1.23 (0.92, 1.65)	0.84** (0.76, 0.94)
SRN	39 1.00	9 0.87 (0.42, 1.79)	17 1.10 (0.62, 1.95)	43 1.94 (1.26, 2.99)	52 2.09 (1.37, 3.17)	1.29** (1.10, 1.51)	8 0.53 (0.25, 1.13)	33 1.30 (0.82, 2.08)	50 2.28 (1.50, 3.47)	29 2.67 (1.65, 4.32)	1.30*** (1.16, 1.46)	20 3.15 (1.86, 5.33)	42 1.89 (1.25, 2.85)	30 1.31 (0.83, 2.06)	29 1.27 (0.75, 2.13)	0.76** (0.65, 0.90)
NSRN	72 1.00	20 1.03 (0.63, 1.70)	35 1.20 (0.80, 1.79)	63 1.58 (1.12, 2.21)	60 1.47 (1.04, 2.09)	1.12 (0.98, 1.27)	29 1.06 (0.69, 1.63)	65 1.46 (1.05, 2.05)	55 1.40 (0.99, 1.99)	29 1.54 (1.00, 2.38)	1.04 (0.93, 1.18)	22 1.94 (1.21, 3.12)	50 1.29 (0.91, 1.83)	56 1.39 (0.99, 1.95)	50 1.35 (0.92, 1.99)	0.91 (0.79, 1.04)
Lung cancer	10 1.00	2 0.75 (0.16, 3.41)	5 1.27 (0.74, 2.20)	18 3.14 (1.45, 6.79)	33 5.05 (2.48, 10.3)	1.66*** (1.31, 2.10)	3 0.77 (0.21, 2.81)	10 1.51 (0.63, 3.62)	26 4.58 (2.21, 9.51)	19 6.70 (3.11, 14.4)	1.40*** (1.20, 1.62)	14 8.68 (4.00, 18.9)	23 4.08 (2.03, 8.20)	15 2.59 (1.21, 5.54)	6 1.00 (0.32, 3.10)	0.53*** (0.40, 0.70)

Note. CHD = coronary heart disease; SRN = smoking-related neoplasm; NSRN = non-smoking-related neoplasm.
^aRate ratios are adjusted for age and grade.
^bChange in mortality (rate ratio) for a given change in the risk factor among ex-smokers.
*P < .05; **P < .01; ***P < .001.

TABLE 5—Effects on Mortality Risk of the Duration of Smoking and the Amount Smoked, for Ex–Cigarette Smokers and Current Smokers Compared with Never Smokers

Duration of Smoking/ Maximum No. of Cigarettes per Day	Ex-Smokers, by Years Since Quitting									Current Smokers	
	≥ 30 y			10–29 y			1–9 y				
	No. of Deaths	RR	(95% CI)	No. of Deaths	RR	(95% CI)	No. of Deaths	RR	(95% CI)	RR	(95% CI)
All causes of death											
≤ 19 y											
1–19 cigs/d	123	0.91	(0.74, 1.11)	42	0.77	(0.56, 1.05)	1[a]	...	...		
≥ 20 cigs/d	66	1.34	(1.04, 1.74)	35	0.99	(0.70, 1.40)	0[a]	...	...		
≥ 20 y											
1–19 cigs/d	36	1.32	(0.94, 1.86)	225	1.24	(1.06, 1.46)	43	1.49	(1.09, 2.04)		
≥ 20 cigs/d	47	1.42	(1.05, 1.92)	279	1.41	(1.21, 1.64)	58	1.69	(1.28, 2.22)		
Current smoking										2.13	(1.92, 2.36)
Coronary heart disease											
≤ 19 y											
1–19 cigs/d	56	1.04	(0.77, 1.40)	15	0.60	(0.35, 1.01)	0[a]	...	...		
≥ 20 cigs/d	26	1.31	(0.87, 1.99)	12	0.74	(0.41, 1.33)	0[a]	...	...		
≥ 20 y											
1–19 cigs/d	9	0.92	(0.47, 1.81)	85	1.18	(0.91, 1.53)	17	1.34	(0.81, 2.21)		
≥ 20 cigs/d	18	1.52	(0.93, 2.47)	111	1.41	(1.11, 1.79)	24	1.60	(1.04, 2.45)		
Current smoking										1.90	(1.62, 2.24)
All neoplasms											
≤ 19 y											
1–19 cigs/d	28	0.80	(0.53, 1.21)	12	0.79	(0.44, 1.44)	1[a]	...	...		
≥ 20 cigs/d	24	1.90	(1.22, 2.95)	15	1.53	(0.89, 2.64)	0[a]	...	...		
≥ 20 y											
1–19 cigs/d	13	1.95	(1.09, 3.49)	62	1.33	(0.98, 1.82)	18	2.30	(1.40, 3.80)		
≥ 20 cigs/d	13	1.61	(0.90, 2.87)	89	1.75	(1.32, 2.31)	22	2.37	(1.50, 3.75)		
Current smoking										2.61	(2.14, 3.18)
Smoking-related neoplasms											
≤ 19 y											
1–19 cigs/d	11	0.90	(0.45, 1.77)	2	0.40	(0.10, 1.64)	0[a]	...	...		
≥ 20 cigs/d	6	1.35	(0.57, 3.18)	6	1.86	(0.78, 4.40)	0[a]	...	...		
≥ 20 y											
1–19 cigs/d	5	1.97	(0.77, 5.03)	18	1.08	(0.61, 1.88)	5	1.82	(0.72, 4.63)		
≥ 20 cigs/d	6	1.97	(0.83, 4.68)	46	2.53	(1.65, 3.88)	15	4.61	(2.54, 8.39)		
Current smoking										4.61	(3.32, 6.39)

Note: RR = rate ratio (adjusted for age and employment grade); CI = confidence interval. The rate ratio for never smokers is 1.0.
[a]Rate ratios not calculated because of small numbers. The expected mortality risk for death from all causes, compared with the risk of never smokers, is less than 1.22.

related neoplasm (rate ratio = 1.63; 95% CI = 1.19, 1.49). This difference could not be explained by their previous smoking habits, as cigarette smokers who switched to a pipe consumed significantly fewer cigarettes, smoked for a shorter period, and had given up smoking for longer than cigarette smokers who gave up all forms of tobacco. Multivariate analysis, controlling for these three factors, increased the relative risks for secondary pipe smokers compared with ex–cigarette smokers. No significant differences were found between secondary cigar smokers and ex-cigarette smokers.

We examined the relationship between smoking status and other potentially confounding variables. Current smokers were more likely to be of lower employment grade, had lower systolic blood pressure, and weighed less than never smokers ($P < .001$). No obvious trend was seen for risk factors between never, ex-, and current cigarette smokers except for grade. The proportion of higher grades (administrative and professional/executive) progressively increased with years since giving up smoking (test for linear trend, $P < .001$). Current pipe smokers had similar profiles regardless of

whether they had smoked cigarettes in the past. Cigar smokers who had never smoked cigarettes had a more favorable risk factor profile except for being shorter in stature (data available on request).

Because smokers may decide to give up their habit because of preexisting disease, we examined the association between smoking habit and four proxy variables suggestive of preexisting cardiovascular, respiratory, and general disease (Table 3). Former smokers were more likely than current smokers to have a doctor diagnosis of heart disease and hypertension, although the prevalence of

electrocardiogram ischemia was similar for both current and former smokers and greater than that for never smokers. The proportions of reported dyspnea and disease at entry were between those of never smokers and current smokers. In general, smokers who had given up smoking within the last 5 years had higher levels of disease or symptoms than longer-term former smokers.

In view of the inconsistent risk factor profile seen with ex–cigarette smokers, we controlled only for age and grade as potential confounders in all subsequent analyses.

Table 4 shows the age- and grade-adjusted rate ratios for ex–cigarette smokers compared with never smokers by (1) the number of years smoked before giving up, (2) the maximum number of cigarettes consumed for a period of at least 1 year, and (3) the number of years since quitting. Among ex–cigarette smokers, a significant increase in mortality compared with that of never smokers was seen only after 20 years of smoking for all-cause mortality; however, the test for trend for duration smoked was significant for all categories of death except non-smoking-related deaths. Significant increases in mortality were seen as the amount consumed increased, except for non-smoking-related neoplasms. Mortality risk fell significantly with years since quitting for all categories except coronary heart disease and non-smoking-related neoplasms. These two categories showed a marked fall after 10 years, but after that period the risks appeared relatively unchanged.

In this cohort, most of the men started to smoke at a similar age. Therefore, among ex–cigarette smokers, for any given age, duration of smoking will determine the number of years since quitting. Hence, these two variables will be highly (negatively) correlated. They will also be correlated with age. In addition, the maximum amount smoked in any year is likely to be higher in those men who smoked the longest. We did not attempt to control for these highly correlated variables simultaneously in a multivariate model because that would require us to make the strong assumption that the effect of each of these factors on the risk of mortality was multiplicative. Instead, to examine the possible effects of the above factors, we carried out a stratified analysis and fitted models by using a dummy variable for each stratum. That allowed the joint effects of the three factors of interest to be assessed relative to men who had never smoked while controlling

for the confounding effects of age and grade (Table 5).

Ex-smokers who never smoked more than 20 cigarettes a day and smoked for less than 20 years showed no evidence of any increased mortality risk for either all-cause mortality or other categories. All-cause mortality remained elevated for heavy smokers who smoked for more than 20 years even after 30 years since quitting. Different patterns emerged for coronary heart disease and neoplasms. Coronary heart disease mortality for former persistent heavy smokers showed an initial fall but then remained at a fairly constant level, although after 30 years this risk was no longer statistically significant. For all neoplasm mortality and smoking-related neoplasm mortality, persistent heavy smokers showed a fall in risk with years since quitting.

Discussion

All-Cause Mortality

Former cigarette smokers had mortality risks between those of current cigarette smokers and those of never smokers, a finding similar to those of other cohort studies.[2–5,7–9] Mortality increased with duration of smoking and maximum amount consumed and decreased with years since quitting. After stratification for these three factors, both the maximum amount smoked and the duration of smoking were independently important in determining mortality risk. Although the risk for ex-smokers fell substantially compared with that for current smokers, persistent heavy smokers showed little further decline with increasing years since quitting. Light smokers who had smoked for less than 20 years had no evidence of any increased risk.

Coronary Heart Disease Mortality

Ex–cigarette smokers showed increased mortality from coronary heart disease compared with never smokers. This mortality risk increased with amount consumed and duration of smoking. A sharp fall in mortality was seen in the first 19 years after quitting. However, after this period there appeared to be little further reduction in risk, and there was no significant trend with years since quitting. Persistent heavy smokers showed a significant elevated risk up to 30 years after quitting.

Several studies have suggested that a risk for coronary heart disease mortality may persist for ex-smokers; however, this

risk was small and not always statistically significant.[4,5,7,8,10] Prospective studies that have examined the effects of years since quitting have noted either a sudden fall in risk with little further decline[7,24] or a slower continual decline.[2–4,10] In general, cohort studies support our finding,[2,3,10] whereas case–control studies suggest that the risk for coronary heart disease mortality or nonfatal infarcts falls quickly with no persistent difference between ex–cigarette smokers and never smokers.[11,12] Both the latter studies have had insufficient power to detect a small excess risk.

Fibrinogen has been shown to be elevated in smokers[25] and is a strong predictor of coronary heart disease.[26,27] The levels for ex–cigarette smokers revert to those of never smokers after several years of cessation.[11,25,28] It is an acute and reversible mechanism by which coronary heart disease risk may change. But persistent heavy smokers may have developed irreversible changes in the coronary architecture, unrelated to fibrinogen. A study of postinfarction angina noted an acute reduction in angina for ex-smokers compared with those who continued to smoke, but no difference by 6 years.[29] The role of a reversible, as well as an irreversible, component may also explain the relatively modest reductions for coronary heart disease mortality seen in intervention trials.[9,30,31]

Neoplasm Mortality

Ex–cigarette smokers showed an elevated risk for neoplasm mortality, lung cancer in particular. Significant trends were seen only for smoking-related neoplasms and lung cancer with amount smoked and duration of smoking. Persistent heavy smokers showed a gradual decline in mortality risk with years since quitting, with the risk after 30 years still raised but no longer statistically significant. A persistent elevated risk for both lung cancer and smoking-related cancers has been seen with both mortality data[4,5,7] and incidence data.[32] Intervention studies, including a subsample of subjects recruited from this cohort, also failed to show a reduction of risk from lung cancer.[9,30] A smoker inhales substances that may act as initiators and promoters of carcinogenesis.[33] Smoking cessation may prevent new lesions from developing but may only retard preexisting early lesions, which continue to develop at a slower rate.

Pipe and Cigar Smokers

Many cohort studies have reported the combined mortality rates of cigar and pipe smokers or have failed to distinguish primary from secondary pipe or cigar smoking.[2,3,5,6,8,10,24,34,35] This distinction is important because smokers from older cohorts are more likely to be primary pipe or cigar smokers, whereas recent cohorts will have more secondary pipe or cigar smokers. A recent study reported that 90% of the cigar smokers were ex-cigarette smokers.[36] The small group of primary cigar smokers showed no evidence of an increased mortality risk compared with never smokers. Both primary and secondary pipe smokers were at greater risk of death from coronary heart disease than cigar smokers. This result contradicts some studies[2-4,37] but is supported by another.[8] Both cigar smoking and pipe smoking have been associated with either a greater risk of coronary heart disease mortality[36-38] or no excess risk.[6,24] These inconsistencies may reflect true differences between populations in the type and amount of tobacco consumed, but more likely they reflect confounding by socioeconomic status or other factors, which will differ for different time periods and countries.

Secondary pipe and cigar smokers had a slightly greater risk of death from coronary heart disease than primary pipe or cigar smokers, as has been noted elsewhere,[10] although this difference was not statistically significant. Higher carboxy-hemoglobin, higher serum cotinine levels, and an increase in fibrinogen levels have been found in secondary compared with primary cigar smokers.[25,39] Secondary pipe or cigar smokers also had greater risks of smoking-related neoplasm death compared with pure pipe or cigar smokers. Although that could have occurred by chance, it is interesting that the rates of non-smoking-related cancers for primary and secondary pipe and cigar smokers were almost identical. This increased risk may reflect a residual carcinogenic effect from cigarettes. In addition, when cigarette smokers change their habit to pipe or cigars they consume more tobacco and inhale to a greater degree.[40] Changing to a pipe was associated with significantly greater mortality than total cessation of smoking, but no real difference was seen for subjects who took up cigar smoking.

With any observational study, it is unclear whether the benefits seen for smoking cessation are due to smoking cessation itself or to other alterations in life circumstances that may occur concurrently. Baseline differences in other risk factors for this cohort showed little consistent pattern apart from socioeconomic status, as in other studies.[41-46] Ex-smokers may pursue a more healthy life-style, but this is probably a more recent phenomenon.[45]

Smoking status was measured only at baseline and may have been misclassified owing to recidivism among ex-smokers. Empirical data from other studies[9,47] suggest that recidivism usually occurs within the first few years of stopping. Heavy smokers are usually,[9,48] but not always,[47] reported as more likely to resume smoking. Recidivism will in general result in an underestimate of the benefits of giving up; however, in the group of heavy smokers who had given up for more than 30 years, this is unlikely to be a serious bias.

Some smokers are likely to give up because of newly diagnosed disease. This is supported by the observation that ex-smokers who had given up smoking for less than 5 years were more likely than current smokers to have a diagnosis of heart disease or hypertension and to complain of dyspnea. These differences were small and are unlikely to explain any persistent risk among ex-smokers who have given up for more than 30 years, although they may result in under-estimating the short-term benefits of giving up.

Conclusions

Ex-smokers show a reduced mortality risk compared with current smokers. This risk may remain persistently higher than the risk for never smokers, depending on previous smoking history and the number of years since quitting. Duration of smoking[10] or consumption of cigarettes[11] alone does not explain the different mortality patterns. Smokers who change to a pipe or cigars appear to retain a greater risk than pipe or cigar smokers who have never consumed cigarettes. Changing to a pipe was associated with a higher mortality risk than that for ex-cigarette smokers who no longer smoked any form of tobacco, but no difference was found for subjects who switched to cigars.

These results have implications for any future predictions about mortality trends for smoking-related diseases. The mortality risk of nonsmokers will differ depending on the proportion of ex-cigarette smokers and their past smoking histories. Hence, the true risk for this group will differ both for different countries and over different time periods. Current life expectancy estimates for ex-smokers[49] may not be valid for future generations.

It is important that the public be aware that whereas stopping smoking results in a markedly diminished risk, a residual excess risk may persist even after many years. The suggestion that ex-smokers have no greater risk than never smokers[50,51] may be counterproductive. Smokers may believe that continuing to smoke is not deleterious as long as they eventually give up. The amount, duration, and period since giving up appear to be important in determining mortality risk. □

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